REMARKS

Claims 1-3 are pending and have been amended.

FORMAL DRAWINGS

The Office Action stated, "The drawing(s) filed on 14 October 2003 is/are: objected to by the Examiner." (Office Action, page 1, box 10). Applicant submits herewith two sheets of formal drawings for Figures 1 and 2. The formal drawings submitted herewith do not raise an issue of new matter.

IDS ENTITLED TO CONSIDERATION

On May 28, 2004, before the date of the Office Action, applicant submitted a Supplemental Information Disclosure Statement (IDS) to make of record an International Search Report issued in connection with the PCT International Application corresponding to the subject application. The May 28, 2004 Supplemental IDS contained the Statement specified in 37 CFR 1.97(e)(1). Accordingly the Supplemental IDS is entitled to consideration. Applicants respectfully request an initialed copy of the Form PTO-1449 submitted therewith.

CLAIMS ARE NOT INDEFINITE

The claims have been rejected under 35 U.S.C. §112, second paragraph. This rejection is respectfully traversed. The Office Action presents four grounds for the rejection, each of which is addressed below.

The first ground of rejection related to the recitation of "A biologically active agent" in the preamble of the independent claim. Although applicant disagrees with the basis of

the rejection, in order to advance prosecution the claims been amended to recite a "compound" as recommended in the Office Action.

Support for the claims as amended may be found, *inter alia,* in the claims as originally filed. Applicant maintains that the amendment does not introduce new matter. The original preamble did not limit the claims. It neither recited essential structure or steps, nor was it necessary to give life, meaning and vitality to the claim, nor did applicant rely on the preamble to distinguish the claimed invention from the prior art. Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808 (Fed. Cir. 2002).

The second ground of rejection is based on the alleged ambiguity of the claim concerning the position of the covalent bond between "A" and the remainder of the compound of Formula III, at least when "A" is a heterocycle. The rejection states:

> Claim 1 . . . recites . . . ". . . the heteroaromatic ring is covalently bound to the remainder of the compound of Formula III by a ring carbon". The claim remains silent about the exact and definite position of covalent bond.

Office Action, paragraph 4. Contrary to the above-quoted assertion, the claim recites that "a ring carbon" of the group "A" is bound to the remainder of the molecule. In accordance with the plain import of the claim recitation, any ring carbon is suitable. Formula III shows that "A" is bound to the remainder of the compound at the $(CH_2)_n$ moiety thereof. The variable "n" can be 1 or 2. When n is 1, "A" must be bound to the only carbon present. When "n" is 2, "A" must be bound to the terminal carbon (i.e. the one that is not directly bound to the O shown in Formula III), because the terminal carbon is the only one of the two carbon atoms that has a valence available for bonding covalently with "A". Thus, the claims clearly and unambiguously define the two carbon atoms that participate directly in the covalent bond at issue.

The third ground of rejection is based on the alleged silence of the claim with regard to the bridge between "A" and the central phenyl ring. The rejection stated, "The Formula

III includes a bridge between components A and the phenyl ring as: ' -(CH2) 1-2 –O- ', whereas the description remains silent about the –CH2- bridge." (Office Action, paragraph 4.) (underlining added). Contrary to the above-quoted assertion, Formula III shows that the $(CH_2)_n$ moiety is bound to "A" on the one side and to the O on the other. Moreover, the claim recites that the variable "n is 1 or 2". Thus, the bridge is clearly and unambiguously defined. If the Office is taking the position that it is necessary for the verbal portion of the claim by itself, without reference to the chemical structure appearing in the claim, to fully address how the bridge is bound to the remainder of the compound of Formula III, such a position would be contrary to the law. The bridge is expressly defined in the claim, which is more than the law requires. Articulate Sys. v. Apple Computer, Inc., 66 F. Supp. 2d 105, 107 (D. Mass. 1999), quoting Morton Int'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470 (Fed. Cir. 1993) ("There is no requirement that each term appearing in the claim be expressly defined in the claim or specification, as long as 'those skilled in the art would understand what is claimed when the claim is read in light of the specification.'"). There is certainly no requirement that the express definition appear or be repeated in the clause of the claim that defines the variable "A".

The fourth ground of rejection is based on the alleged ambiguity with regard to whether the heterocycle is substituted or unsubstituted. The rejection asked, "Also, are substituents on to the heterocycle(s) excluded?" (Office Action, paragraph 4.) The specification and claims consistently use the terms "unsubstituted or substituted" or "substituted" when the group in question can or must be substituted. When the group is not substituted, the specification and claims simply name the group without adding the adjective "unsubstituted." Thus, for example claim 1 recites "alkyl having 1 or 2 carbon atoms," and the Office implicitly acknowledges that there is no ambiguity about whether that alkyl group is or is not further substituted. Similarly, the person of ordinary skill in the art would understand that "a 5 or 6 membered heteroaromatic ring" does not literally read on a 5 or 6 membered heteroaromatic ring bearing additional substituents beyond those actually shown in the formula.

In view of the amendment and the preceding remarks applicant respectfully maintains that the rejection under Section 112, second paragraph, has been overcome and should be withdrawn.

INVENTION IS NOVEL OVER U.S. PATENT NO. 4,845,231

Claims 1-3 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 4,845,231 (Kees), also cited as Chemical Abstract DN 111:232835. This rejection is respectfully traversed.

The rejection relies on the compound having Chemical Abstracts Reference No. 123891-91-8. Referring to the nomenclature utilized in the claims, in the reference compound the variable "A" is a cycloalkyl. However in the claims as currently amended "A" is a phenyl (claims 1-3) or a heteroaromatic (claim 1), but not cycloalkyl. Accordingly, the reference compound does not anticipate the claims.

INVENTION IS NONOBVIOUS OVER MUSSER AND SOHDA

Claims 1-3 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Musser, et al. (J. Med. Chem., 33/1, 240-245 (190) (also cited as Chemical Abstract DN 112:35651) and EP 0 629 624 (Sohda, et al.) (also cited as Chemical Abstract DN 123:143900), either in combination or over each of them taken separately. Full length versions of the Musser, et al. and Sohda, et al. references are enclosed herewith. In the following remarks, applicant addresses in turn, Musser alone, Sohda alone, and the combination of Musser and Sohda.

Musser reports the results of a structure-activity study on a series of leukotriene D4 antagonists, which are said to have activity against bronchoconstriction. Referring to the nomenclature of the claims in the subject application, in the Musser compounds "A" is always a bicyclic group. See Table 1 of Musser on page 242. Musser varies the number

of ring atoms, and whether the bicycle contains 0, 1 or 2 heteroatoms, and the identity of such heteroatoms. Musser also varies the identity of R^1 (see Musser, Table 1), which is in the same position as the tetrazolemethyl group in the invention of this application. But Musser does not vary the presence of a bicyclic group for "A". The rejection does not, because it cannot, present any reasoning to support the proposition that the person of ordinary skill would have been motivated, upon reading Musser, to substitute a monocyclic heteraromatic ring for the bicyclic rings disclosed in Musser. Why did Musser, et al. not even test the monocyclic heteroaromatic analog of the lead compound? Because they did not have a reasonable expectation that the monocyclic analog would possess the desired pharmacological activity. Nor would the person of ordinary skill in the art.

Sohda discloses a number of compounds that are said to have hypoglycemic and hypolipidemic action. In the reference compounds cited by the rejection (Chemical Abstracts Reference No. 166253-98-1 and No. 166254-03-1) as well as all of the compounds listed in Tables 4 through 8, the heteraromatic ring "A" is always substituted, and usually disubstituted. In contrast, in the instant invention the heteraromatic ring is unsubstituted, as discussed above in connection with the Section 112, second paragraph, rejection. In view of the preference of Sohda for substituted heteroaryl groups, the person of ordinary skill in the art would not have been motivated to substitute an unsubstituted oxazolyl for the substituted oxazolyl in the cited reference compounds.

Sohda discloses and claims a genus of compounds that do not generically encompass the compounds claimed by applicant because of the length of the bridge "Y". (See Sohda, page 5, lines 1-38 and claim 1.) Referring to the Sohda nomenclature, in the Sohda genus "Y" is $-CH_2CH_2CH_2-$ or $-CH_2CH_2CH_2CH_2-$, whereas in the claimed invention "Y" is $-CH_2-$. The rejection wrongly alleges that the claimed compounds are adjacent homologs. The rejection states:

> It cannot be ignored that prior art(s) . ... are involving the concept of adjacent homologies consisting of –CH2- group. . . . Applicants'

> compounds are forming lower homologue(s) tha[n] the ref. Compounds (in that the instant compounds have limited the –CH2- bridge to 1 or 2 . . . ."

Office Action, paragraph 11. Contrary to the above-quoted passage, in the claimed compounds the bridge "Y" does not contain 2 methylene units. Rather it contains a single methylene unit. Thus, the claimed compounds are not adjacent homologs of the Sohda genus, in which the bridge "Y" contains 3 or 4 methylene units.

The claims are not obvious over the combination of Musser and Sohda. In the Musser compounds variable "A" is invariably a bicyclic. In the specific compounds of Sohda cited in the rejection the heteroaromatic ring "A" is always substituted. Assuming, for the sake of argument, that the person of skill in the art would have been motivated to look to the combination of Musser and Sohda, the rejection does not present any reasoning to explain how the combined teaching of bicyclic heteroaromatic compounds by Musser and substituted heteroaromatic compounds by Sohda would have suggested unsubstituted heteroaromatic compounds as claimed in the instant invention.

It is true, that one could select unsubstituted heterocyclics from the Sohda genus for "A" and combine them with moieties selected from the Musser compounds to arrive at compounds having the same "n" value as applicants' claimed invention. But someone, like the PTO or an accused infringer, who has the burden of establishing obviousness "cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention." SmithKline Diagnostics, Inc. v. Helena Laboratories Corp., 859 F.2d 878, 887, 8 USPQ2d 1468, ____ (Fed. Cir. 1988). The rejection does not explain why the combination of individual elements from two compounds having different pharmaceutical activities would have been expected to result in a compound with pharmaceutical activity.

Moreover, the rejection does not explain how the person of ordinary skill in the art "with no knowledge of the claimed invention" (In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d

1313, ____ (Fed. Cir. 2000)) would have known the right elements to pick and choose from the prior art compounds. Without the hindsight provided by applicants' invention, there would have been no suggestion or motivation to comb through the prior art, selecting specific elements and combining them in just the right way so as to arrive at the claimed invention. Accordingly, applicant respectfully maintains that the claims are patentable over the Musser, et al. and Sohda, et al. references, whether taken separately or together.

CONCLUSION

In view of the amendments and the preceding remarks, applicant submits that the subject application is now in condition for allowance. Reconsideration and withdrawal of all objections and rejections is respectfully requested.

It is believed that no fee is required in connection with the filing of this Amendment. If any fee is required, the Commissioner is hereby authorized to charge the amount of such fee to Deposit Account No. 50-1677.

Respectfully submitted,

Lewis J. Kreisler
Reg. No. 38522
Attorney for Applicant(s)

930 Clopper Road
Gaithersburg, MD 20878
Phone: (240) 631-2500 x3276
Facsimile: (240) 683-3794

Enclosures: Formal drawings (2 sheets).
Musser, et al., J. Med. Chem., 33: 240-245 (1990).
EP 0 629 624 B1 (Sohda, et al.)